Chapter 13

Acute Metabolic Complications in Diabetes

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SUMMARY

The acute metabolic complications of diabetes consist of diabetic ketoacidosis (DKA), hyperosmolar non-ketotic coma (HNC), lactic acidosis (LA), and hypoglycemia. DKA and HNC are related to insulin deficiency. Hypoglycemia results from the treatment of diabetes, either with oral agents or insulin. Although hypoglycemia may occur in conjunction with oral hypoglycemic therapy, it is more common in patients treated with insulin. LA is usually associated with other factors that may be related to diabetes, such as cardiovascular disease (acute myocardial infarction) associated with hypoxia and excess lactic acid production.

The incidence rate for DKA varies with definition, age, and sex. The rate from population-based studies ranges from 4.6 to 8 per 1,000 diabetic persons per year. It is more common in young diabetic people and may be more common in women than men. DKA may be the initial manifestation of diabetes in 20%-30% of cases. Incidence rates for HNC, LA, and hypoglycemia are not available from population-based studies. Hypoglycemic events varied in the Diabetes Control and Complications Trial (DCCT) between the treatment groups. These events were associated with the degree of normalization of glycemia.

Precipitating factors for DKA, HNC, and LA include acute illness or co-morbidity such as cardiovascular disease, injury or infection, medications, and poor compliance or errors in compliance with treatment. Precipitating factors for hypoglycemia include dosage of oral hypoglycemic agent or insulin; errors in dosage administered; timing of the medication, particularly insulin; delay in meals; and co-morbidity such as renal insufficiency, adrenal insufficiency, and pituitary insufficiency. Prevention of these acute complications remains an important element in their management. Recognition of precipitating factors and appropriate instruction, awareness, and self-care will decrease the occurrence of these complications.

DKA, HNC, and LA require hospitalization for treatment and thereby result in the use of significant health care resources with increased health care costs. Prevention is an important component in reducing health care cost for these disorders. Hypoglycemia can usually be treated in an ambulatory care setting without using significant health care resources. Severe hypoglycemia with loss of consciousness may necessitate hospitalization, however.

Significant morbidity and mortality is associated with DKA, HNC, and LA. Prompt recognition and management of these disorders and their associated morbidity results in improvement. Mortality rates are ~9%-14% for DKA and 10%-50% for HNC. The mortality rate for LA is >50% with serum concentrations of lactic acid >5 mmol/L when associated with circulatory failure or septic shock. Hypoglycemia is usually associated with symptoms that are reversible with prompt treatment. Severe and profound hypoglycemia may be associated with long-term neurologic impairment.

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DIABETIC KETOACIDOSIS

DKA is one of the major acute diabetic complications. It usually occurs in the context of total insulin deficiency, such as in insulin-dependent diabetes mellitus (IDDM). It occurs rarely in non-insulin-dependent diabetes mellitus (NIDDM) under the stress of acute illness. When DKA occurs in patients with NIDDM, it may represent a transition to insulin deficiency.

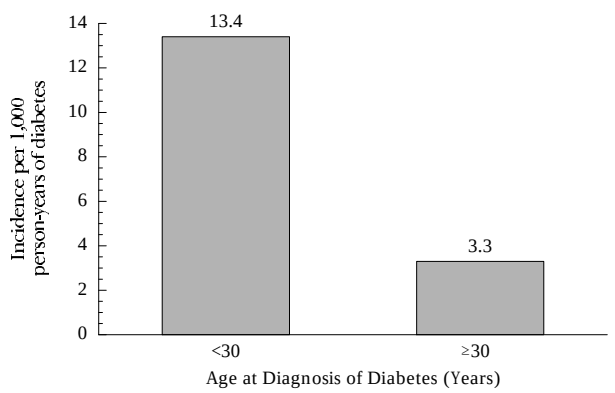
DEFINITION

DKA is clinically defined by absolute insulin deficiency with hyperglycemia (glucose levels usually >200 mg/dl) with increased lipolysis, increased ketone production, hyperketonemia (ketone levels positive at 1:4 dilution of serum or greater or beta hydroxybutyrate >0.5 mmol/L), and acidosis (pH ≤7.3 or bicarbonate ≤15 mEq/L). Normoglycemic ketoacidosis has been reported and milder forms of ketoacidosis have also been described with bicarbonate levels between 15-18 mEq/L. It is important to precisely define DKA in epidemiologic studies to accurately assess and compare morbidity and mortality.

INCIDENCE

The incidence of DKA depends on its definition and its recognition and ascertainment from hospital records and hospital discharge summaries. Because of the acuteness and severity of the disorder, it is likely to be recognized and easily ascertainable. However, varying diagnostic levels of pH and bicarbonate may result in over- or under-diagnosis of the disorder. In community-based studies, such as in Rochester, MN and Rhode Island, there were definitive criteria used for the diagnosis of DKA[1,2]. The incidence rate in Rochester, MN varied from 8 per 1,000 person-years for DKA at all ages to 13.4 per 1,000 person-years among diabetic persons who had the diagnosis of diabetes made at age <30 years (Figure 13.1). The Rhode Island Hospital Study estimated the incidence of DKA at 4.6 per 1,000 diabetic persons per year, with the rates being highest in the youngest age group (Figure 13.2). The rate was higher in women than men with diabetes.

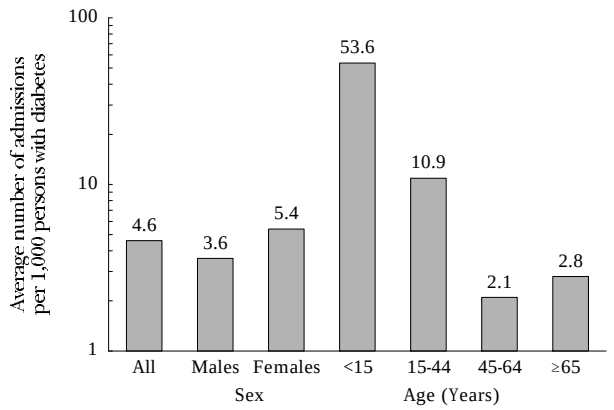
Figure 13.1
Incidence of Diabetic Ketoacidosis in Patients with Diabetes, Rochester, MN, 1945-70



Data are shown as number per 1,000 person-years. A central file of all medical, surgical, and pathologic records of Rochester residents were reviewed to ascertain diabetes (n=1,536) and to ascertain a diagnosis of diabetic ketoacidosis (n=92) in this community-based study of diabetes.

Source: Reference 1

Figure 13.2
Annual Incidence of Hospital Admissions for Diabetic Acidosis per 1,000 Estimated Diabetic Persons, Rhode Island, 1979-80



All admissions meeting diagnostic criteria for diabetic acidosis to all acute care hospitals in Rhode Island were included (n=152). Population estimates of diabetes were obtained from the 1981 Rhode Island Diabetes Control Program survey and a 1980 statewide household interview survey.

Source: Reference 2

The diagnosis of DKA was found as the initial manifestation of diabetes in 20% of patients in the Rhode Island study[2] and in 26% of patients with diabetes onset at age <30 years and 15% of those diagnosed at age ≥30 years in the Rochester, MN study[2]. The median time from diagnosis of diabetes until the patient presented with DKA was 4.6 years in those patients not initially presenting with DKA[1]. This median time varied by age of diagnosis of diabetes, being 1.8 years in persons diagnosed at age <30 years and 9.1 years when age of diagnosis was ≥30 years[1].

Repeat hospitalizations for DKA were observed in 15% of all diabetic admissions to Rhode Island hospitals in 1979-80[2]. In the population-based study of Rochester, MN, 33 of 79 diabetic patients surviving a first episode of DKA had at least one subsequent episode[1].

PRECIPITATING FACTORS

DKA may be the initial manifestation of diabetes, particularly for IDDM, in 20%-30% of cases of DKA. Precipitating factors for DKA in those with established diabetes include infection, other acute illnesses, lack of diabetes education and training, noncompliance, poor self-care, inadequate glucose monitoring, psychological problems, and indeterminate causes[1-6]. Infection is a commonly cited precipitating

factor. Very often, no known precipitating factor can be identified, but under these circumstances, it is most likely related to poor compliance, poor self-care habits, and unrecognized subclinical illness. A recent study reported that persons without health insurance or with only Medicaid reimbursements had hospitalization rates from DKA that were two to three times higher than comparable rates among diabetic persons who had private health insurance[7]. As part of a set of overall influencing factors, the type of health insurance may be one factor leading to these hospital admissions.

PREVENTION AND TREATMENT

Prevention remains the most important aspect of managing DKA in known diabetic persons. This prevention can be accomplished through appropriate education, improved self-care and compliance, and self-monitoring of blood glucose. A few studies have shown reductions in DKA hospitalizations accompanying patient education, follow-up care, and increased access to medical advice[8-10]. In ambulatory programs having improved patient access to medical care and providing outpatient education, there has been a 40%-50% reduction in diabetes hospitalizations among patients who attended classes[8-9]. For culturally diverse populations, sensitivity to ethnic and cultural needs of the respective populations is an important aspect of delivering health care to reduce DKA incidence.

More attention in the ambulatory care setting to diabetes education, self-care, and self-blood glucose monitoring should result in decreased frequency of DKA and decreased hospitalizations for the condition. Reducing hospitalizations for DKA will decrease the cost burden of health care delivery in diabetes. Preventive actions in known diabetic patients can ease the economic burden of DKA.

DKA as an initial manifestation of IDDM is less amenable to prevention, other than through appropriate surveillance in high-risk patients and awareness and recognition of the disorder.

For an individual patient, attention to clinical and laboratory values will dictate the appropriate treatment of DKA. In clinical practice, the recognition of impending or actual DKA and prompt treatment are key to management. Milder forms of the disorder can be recognized in the ambulatory care setting and can be corrected promptly in that setting without the need for hospitalization. The more severe forms of DKA require hospitalization for initiation of intravenous therapy and correction of the acid-base and electrolyte disturbances. Use of continuous intravenous insulin therapy has reduced the frequency of post-treatment hypokalemia. Attention to hydration and to acid-base and electrolyte management has resulted in fewer post-treatment electrolyte disturbances, such as hypokalemia and hypophosphatemia. The treatment remains hydration, insulin therapy, and electrolyte repletion.

Table 13.1
Hospitalizations for Acute Complicaton of Diabetes, U.S., 1989-91

Complication (ICD9-CM code) and age (years)	Average annual number of discharges for complication (thousands)	Percent of total diabetes discharges*
Diabetic ketoacidosis (250.1)		
<17	16.9	41.2
18-44	48.9	14.1
45-64	20.4	2.4
≥65	14.0	0.8
All ages	100.2	3.4
Diabetic coma NEC (250.3)		
<17	0.2	0.5
18-44	0.5	0.1
45-64	1.1	0.1
≥65	2.7	0.2
All ages	4.5	0.2
Diabetic hyperosmolar coma (250.2)		
<17	0.2	0.5
18-44	0.9	0.3
45-64	1.9	0.2
≥65	7.8	0.5
All ages	10.8	0.4
Acidosis (276.2)		
<17	0.6	1.5
18-44	1.7	0.5
45-64	7.1	0.8
≥65	9.4	0.6
All Ages	18.8	0.6
Hypoglycemic coma (251.0)		
<17	0.1	0.2
18-44	1.6	0.5
45-64	2.9	0.3
≥65	8.5	0.5
All ages	13.1	0.5
Hypoglycemia NOS (251.2)		
<17	1.1	2.6
18-44	6.6	1.9
45-64	9.5	1.1
≥65	31.3	1.9
All ages	48.5	1.7

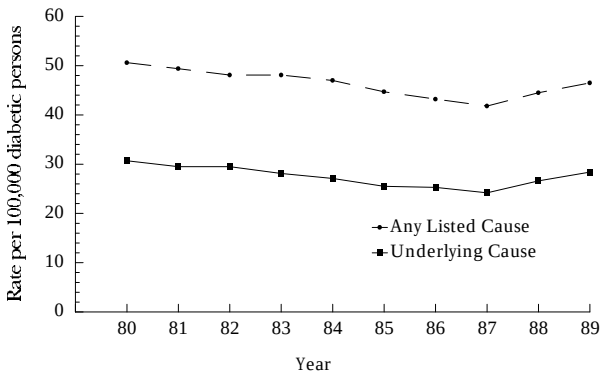
* Total average annual number of discharges (in thousands) with any diabetes diagnosis in 1989-91 were age <17 years, 40.9; age 18-44 years, 346.8; age 45-64 years, 855.0; age ≥65 years, 1682.4; all ages, 2925.1. ICD9-CM codes used to identify diabetes hospitalizations were 250.00-250.92, 251.3, 357.2, 362.00-362.02, 366.41, 648.00-648.04, and 775.10 as any diagnosis listed on the hospital discharge record.

Source: U.S. National Hospital Discharge Survey, National Center for Health Statistics

HOSPITAL DISCHARGE DATA AND ECONOMIC IMPACT

DKA results in the use of significant health care resources, which increase health care costs. In 1983, the cost of hospitalization in one year for diabetic ketoacidosis in Rhode Island was estimated to be $225 million. It was further estimated that 50% of these hospitalizations could have been prevented by better adherence to self-care and compliance with diabetes management programs. Data for DKA and diabetic coma from U.S. hospital discharge surveys are shown in Tables 13.1 and 13.2. Unfortunately, these data do not provide the biochemical criteria on which the diagnosis was based or the precipitating causes. There were an annual average of ~100,000 hospitalizations in which DKA was listed and 4,500 in which diabetic coma was listed during 1989-91. DKA represents only 0.3% of all hospitalizations and 3.4% of diabetic hospitalizations. About 52% of DKA hospitalizations were in females, 61% in Caucasians, and 23% in African Americans. About 41% of all diabetes discharges in 1989-91 for patients age <17 years were for DKA (Table 13.1). The number of DKA hospital discharges was highest for persons age <45 years. Discharge rates were highest for black males and were similar for black females, white females, and white males. There is no apparent national or regional trend or variation for DKA that is discernable from current hospital discharge data[11].

Figure 13.3
Age-standardized Mortality Coded to Diabetic Ketoacidosis, U.S., 1980-89



Numbers of deaths are derived from death certificates in the U.S. listing ICD 250.1 as either the underlying cause or any listed cause of death. Rates are shown per 100,000 estimated diabetic population. Estimates of the diabetic population were obtained from the National Health Interview Survey.

Source: Reference 11

MORBIDITY AND MORTALITY

Morbidity associated with DKA relates to the severity of the acid-base and electrolyte disturbances. These disturbances may result in coma and death. A serious post-treatment complication is cerebral edema, which may be related to therapy[12]. It is important to correct slowly the hyperglycemia, acidosis, and electrolyte disturbances to prevent precipitating cerebral edema. With the increased use of continuous intravenous insulin infusion and with gradual improvement in glycemia, cerebral edema occurs less frequently.

Interpretation of death certificate data related to DKA is difficult, as very often another condition may be the underlying cause of death, such as acute myocardial infarction or sepsis. The mortality rate for DKA was 14% for the initial episode of DKA in the population-based study in Rochester, MN[1]. Eleven percent died during a subsequent DKA. The mortality rate estimated from the Rhode Island Hospital Study was 9%[2]. Mortality rates for patients with DKA vary from 5%-45%[1-4,12,13]. DKA was reported as the underlying cause of death for 1,905 deaths in 1988[14]. During 1980-89, age-standardized DKA underlying cause mortality rates varied slightly from 30.7 to 24.2 per 100,000 diabetic population (Figure 13.3). Highest rates occurred in those age >75 years (Figure 13.4). Age-standardized mortality rates were highest for black males, intermediate for black females, and lowest for

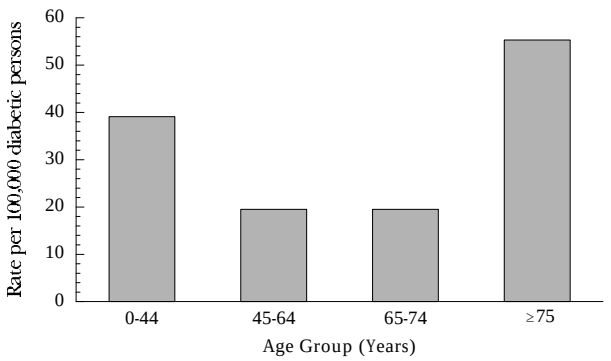
Table 13.2
Average Annual Number of Hospital Discharges Listing Diabetic Ketoacidosis (ICD 250.1) and Diabetic Coma (ICD 250.3), U.S., 1989-91

Diagnosis	Number (thousands)	Percent of all hospitalizations	Percent of diabetes hospitalizations	Female (%)	White (%)	Black (%)	Other/unknown race (%)
All hospitalizations	34,720	100		60	68	12	20
Diabetes	2,925	8.4	100	57	69	15	16
Diabetic ketoacidosis	100	0.3	3.4	52	61	23	16
Diabetic coma	4.5	0.0	0.2	58	65	16	19

Data for all hospitalizations were for 1990 and for diabetic hospitalizations were for 1989-91.

Source: U.S. National Hospital Discharge Survey, National Center for Health Statistics

Figure 13.4
Mortality Coded to Diabetic Ketoacidosis, by Age at Death, U.S., 1989



Numbers of deaths are derived from death certificates in the U.S. listing ICD 250.1 as the the underlying cause of death. Rates are shown per 100,000 estimated diabetic population. Estimates of the diabetic population were obtained from the National Health Interview Survey.

Source: Reference 11

whites, with no difference among whites between males and females[11].

HYPEROSMOLAR NON-KETOTIC COMA

DEFINITION

HNC is clinically defined by the presence of relative insulin deficiency and hyperglycemia, usually >1,000 mg/dl with associated elevated serum osmolality (>300 mosm/kg), dehydration, and stupor, progressing to coma if uncorrected, without the presence of ketosis or acidosis. These patients have sufficient circulating insulin to prevent lipolysis and ketosis.

INCIDENCE AND PRECIPITATING FACTORS

Unfortunately, there are no population-based studies for HNC. It occurs rarely and is clinically associated with NIDDM. Typically, in clinical practice, HNC is seen in patients with NIDDM and residual insulin secretion[4]. HNC is reported to occur more often in Caucasians and females.

Hospitalization data confirm that HNC occurs rarely (Tables 13.1 and 13.3) and is most commonly seen in individuals age >65 years (Table 13.1).

The usual precipitating factors are dehydration, medications such as steroids and thiazides, acute illness, cerebral vascular disease, advanced age, and, rarely, new diagnosis of diabetes.

Table 13.3
Average Annual Number of Hospital Discharges Listing Hyperosmolar Nonketotic Coma (ICD 250.2), U.S., 1989-91

Race or sex group	Number (thousands)	Percent of all diabetes hospitalizations*	Percent of all hospitalizations*
Total	10.8	0.37	0.03
White	6.3	0.31	0.03
Black	2.9	0.66	0.07
Other/unknown race	1.5	0.33	0.02
Male	3.7	0.30	0.03
Female	7.1	0.42	0.03

* Percent of hospitalizations in the race or sex group.

Source: U.S. National Hospital Discharge Survey, National Center for Health Statistics

PREVENTION AND TREATMENT

Prevention of HNC in known diabetic persons is accomplished through education, self-monitoring of blood glucose, self-care, avoidance of dehydration, and awareness and avoidance, if possible, of medications that may precipitate the disorder, such as steroids and thiazides.

Patients with HNC respond well to hydration and small doses of insulin to correct hyperglycemia. Hospitalization is usually short unless there is some underlying or co-morbid condition that prolongs the stay. There is no evidence that any regional variation exists in the occurrence of HNC. Some patients with HNC may be treated in the ambulatory care setting before they lapse into more severe mental status disorientation.

MORBIDITY AND MORTALITY

Morbidity of HNC consists of coma and impaired neurologic function with a predisposition to vascular occlusive disease from dehydration or poor perfusion. Cerebral edema may also occur as a complication of treatment with rapid correction of the hyperglycemia. Continuous insulin infusion with gradual correction of hyperglycemia should obviate the complication of cerebral edema[15].

Mortality attributed to HNC is variable, with rates from 10%-50%, most likely depending on the underlying illness or co-morbidity[15,16].

LACTIC ACIDOSIS

DEFINITION

LA consists of elevated lactic acid (lactic acidemia, ≥2.0 mmol/L) with acidosis (pH ≤7.3) and without ketoacidosis. There may be low levels of ketones present (≤1:4 on serum dilution, or beta hydroxybutyrate >0.4 but <0.6 mmol/L). Approximately half of the reported cases of LA have occurred in patients with diabetes[17]. Currently, LA is rarely seen in diabetic patients, particularly since the withdrawal of phenformin from the market.

Occasionally a combined LA and DKA may be present. In this situation, the presence of excess lactate may decrease production of acetoacetate, which is measured by dipstick methods for ketones, but beta hydroxybutyrate levels may remain elevated with an increased ratio of beta hydroxybutyrate to acetoacetate. Under the circumstances of combined LA and DKA, LA predominates by laboratory parameters and may mask an associated or underlying DKA.

INCIDENCE AND PRECIPITATING FACTORS

There are no data on incidence rates for LA. The ICD-9 code 276.2 identifies acidosis, primarily lactic acidosis. Hospitalizations in 1989-91 with this code in patients with and without a concomitant diagnosis of diabetes are shown in Tables 13.1 and 13.4. Most LA occurred in individuals age >45 years, in women, in Caucasians, and in patients for whom diabetes was not listed on the hospital discharge summary.

The usual precipitating factors for LA are hypoxia and some medications, such as phenformin. Phenformin, a biguanide, is no longer available in the United States because of its predisposition to the development of life-threatening LA.

PREVENTION AND TREATMENT

Prevention of LA is difficult. Often the predisposing conditions, such as acute myocardial infarction with hypoxia, or septic shock, are acute events and may not be amenable to immediate prevention other than through long-term prevention of degenerative disease or sepsis through control and modification of risk factors. LA does not usually occur in conjunction with poorly regulated diabetes unless there is some additional insult that produces hypoxia.

Treatment of LA is essentially the same whether alone or in combination with DKA in terms of hydration, restoration of electrolyte balance, correction of acidosis, and correction of hyperglycemia, if present. Rapid correction of hyperglycemia and the acid-base balance may result in cerebral edema in susceptible individuals. Therefore, patients should be carefully monitored with prompt but gradual correction of the abnormal pathophysiology.

The key issue in management is physician awareness of the disorder and correct interpretation of laboratory studies. The clinical clue that the patient has LA as opposed to DKA will depend on the laboratory findings and clinical awareness that both conditions may co-exist, and that LA may result in modification of the laboratory findings, in terms of measured ketone levels by dipstick, and that correction of acid-base and electrolyte disturbances may be more difficult with LA.

Patients with LA are usually hospitalized. Their hos-

Table 13.4
Average Annual Number of Hospital Discharges Listing Lactic Acidosis (ICD 276.2), U.S., 1989-91

	Diabetes			No diabetes	
Race or sex group	Number (thousands)	Percent of all diabetes hospitalizations*	Percent of all hospitalizations*	Number (thousands)	Percent of all nondiabetic hospitalizations*
Total	18.8	0.6	0.05	107.8	0.3
White	12.3	0.6	0.05	71.1	0.3
Black	3.8	0.9	0.09	18.2	0.5
Other/unknown race	2.6	0.6	0.03	18.5	0.3
Male	6.6	0.5	0.05	46.9	0.4
Female	12.2	0.7	0.06	60.9	0.3

* Percent of hospitalizations in the race or sex group. Data for all hospitalizations were for 1990 and for diabetic hospitalizations were for 1989-91.

Source: U.S. National Hospital Discharge Survey, National Center for Health Statistics

pitalization may be prolonged because of the underlying condition that may have led to the LA. The economic impact will be considerable, as these patients will spend several days in the hospital under carefully monitored conditions.

MORBIDITY AND MORTALITY

The major morbidity associated with LA is neurologic impairment and possible cerebral edema with rapid correction of the acid-base and electrolyte disturbances. Whether there is a predisposition to vascular complications related to dehydration or hypoxia is unclear.

The mortality rate from LA is high. The higher the lactic acid level in association with the acidosis, the higher the mortality rate. LA accounts for a very small portion of the total mortality in diabetic patients.

HYPOGLYCEMIA

DEFINITION

Hypoglycemia is common in insulin-treated diabetic patients and also occurs occasionally in patients treated with the oral hypoglycemic sulfonylurea agents. Hypoglycemia may range from very mild lowering of glycemia (60-70 mg/dl) with minimal or no symptoms, to severe hypoglycemia with very low levels of glucose (<40 mg/dl) and neurologic impairment. Glucose levels of 40-70 mg/dl usually can be treated with oral carbohydrate and would not require further medical attention. More severe hypoglycemia (glucose levels <40 mg/dl) may require intervention with either intravenous glucose or glucagon, but the patient may be sufficiently responsive to take oral carbohydrate to relieve the hypoglycemia.

INCIDENCE AND PRECIPITATING FACTORS

Patients with more severe hypoglycemia are more likely to need medical attention and thus are more readily ascertained for demographic analysis. These patients will usually represent what is reported for the frequency of hypoglycemia in a diabetic cohort. The incidence of hypoglycemia will also vary with the definition of the glucose level and the clinical recognition of symptomatic hypoglycemia. Therefore, the incidence of hypoglycemia cannot be adequately ascertained. In the DCCT, the incidence of adverse significant hypoglycemic events was 6% in the intensively treated group[18]. It is most likely lower in the general diabetic population, as the hypoglycemia occurring in the DCCT was related to the intensity of the insulin therapy program. Most patients are not as intensively treated or compliant with treatment as were the DCCT patients.

Tables 13.1 and 13.5 show the frequency of the discharge diagnosis of hypoglycemia (ICD 251.2) for hospitalizations in the United States in 1989-91. About 64% of hospitalizations for hypoglycemia listed diabetes in the discharge summary and 36% did not. Hypoglycemia represented a greater proportion of hospitalizations for females and African-American patients with diabetes (Table 13.5). Most hospital discharges for hypoglycemia in diabetic patients occurred in patients age >65 years (Table 13.1). There is no apparent regional variation in the occurrence of hypoglycemic episodes[11].

An additional 0.45% of diabetes hospitalizations and 0.01% of hospitalizations without diabetes involved hypoglycemic coma (ICD 251.0)(Tables 13.1 and 13.5). No definition for the diagnosis of hypoglycemia and hypoglycemic coma is available for these hospital discharge diagnoses, but these are clinical diagnoses provided by the attending physician at the time of discharge. Hypoglycemic coma was also more common in discharges for women and African-Americans with diabetes.

Hypoglycemia associated with insulin therapy may be related to errors in dosage, delayed or skipped meals, exercise, intensity of glycemic control, variation in absorption of circulating insulin from subcutaneous depots, variability of insulin binding, degradation and action, impairment of counter regulation, and possibly the use of human insulin. Impairment of counter regulation and autonomic neuropathy contributes to hypoglycemic unawareness, which further complicates insulin therapy in diabetes management and glycemic control. The frequency of hypoglycemic events is increased in diabetic patients who have renal, adrenal, or pituitary insufficiency.

PREVENTION AND TREATMENT

Frequent self-monitoring of blood glucose should reduce the frequency of hypoglycemic reactions, but not necessarily, as noted in the DCCT study[18]. It is important for the patient with diabetes to avoid missing meals after taking insulin. Also, adjustments for exercise, either by additional food intake or adjustment of insulin dosage, will need to be made to avoid hypoglycemia. Multiple daily doses of insulin make it possible

Table 13.5
Average Annual Number of Hospital Discharges Listing Hypoglycemia (ICD 251.2) and Hypoglycemia Coma (ICD 251.0), U.S., 1989-91

Race or sex group	Diabetes			No diabetes	
	Number (thousands)	Percent of all diabetic hospitalizations*	Percent of all hospitalizations*	Number (thousands)	Percent of all nondiabetic hospitalizations*
Hypoglycemia					
Total	48.5	1.6	0.14	26.9	0.09
White	29.7	1.5	0.13	17.2	0.08
Black	13.5	3.0	0.32	5.1	0.14
Other/unknown race	5.4	1.3	0.08	4.6	0.08
Male	18.6	1.5	0.13	12.0	0.09
Female	29.9	1.8	0.15	14.9	0.08
Hypoglycemic coma					
Total	13.1	0.45	0.04	3.4	0.01
White	8.2	0.40	0.03	1.4	0.01
Black	3.9	0.87	0.09	0.2	0.01
Other/unknown race	1.0	0.23	0.01	1.8	0.03
Male	5.4	0.44	0.04	1.5	0.01
Female	7.7	0.46	0.04	1.7	0.01

* Percent of hospitalizations in the race or sex group. Data for all hospitalizations were for 1990 and for diabetic hospitalizations were for 1989-91.

Source: U.S. National Hospital Discharge Survey, National Center for Health Statistics

to adjust the insulin program for possible delays in meals or unplanned exercise.

Prevention of hypoglycemia depends on appropriate education regarding diabetes management and self-care, self-monitoring of blood glucose, and awareness of factors that may precipitate hypoglycemia.

Patients with NIDDM who develop hypoglycemia while on sulfonylurea therapy are usually age >60 years and may have some mild renal insufficiency. It is therefore important to treat individuals age >60 years cautiously with sulfonylureas and modify the dosage upward, as needed, for glycemic control. It is rarely necessary to aggressively treat elderly patients to precipitously correct hyperglycemia to normal glycemia.

Patients do not usually require hospitalization for hypoglycemia unless it is extremely severe and/or the patient becomes unresponsive. Oral carbohydrate in a readily available form and/or glucagon therapy is sufficient to correct the hypoglycemia and restore the patient to euglycemia without hospitalization. Intravenous glucose can also be given in an outpatient setting or by paramedical assistants. Obviously, the use of intravenous glucose and the need for monitoring after a severe hypoglycemic episode may necessitate temporary hospitalization, which will increase cost.

MORBIDITY AND MORTALITY

The major morbidity associated with hypoglycemia is temporary neurologic deficit and coma, seizures with central nervous system injury, and permanent neurologic impairment if treatment is delayed or omitted. This morbidity is important in children, who appear to be more sensitive to hypoglycemia with the occurrence of electroencephalographic changes and seizure episodes. Often it is difficult to separate an underlying seizure disorder from hypoglycemic episodes. The key, again, is careful monitoring and adjustment of insulin dosage to avoid the extremes of hyperglycemia and hypoglycemia.

Death related to hypoglycemia in diabetes occurs rarely. There were none recorded in the DCCT[18]. Among patients using insulin pump therapy, there was only one death reported related to hypoglycemia[19]. The majority of patients with hypoglycemia survive the episode.

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